REMARKS

Claims 13-16 are all the claims pending in the application; each of the claims has been rejected.

Upon entry of this amendment, claim 16 will be canceled and claims 13-15 will be pending.

No new matter has been added. Entry of the Amendment is respectfully requested.

I. Rejection of Claims Under 35 U.S.C. §112

A. At page 2 of the Office Action, claims 13, 14, and 16 are rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. The Examiner notes that this is a new matter rejection.

The Examiner states that the specification does not provide support for amendment of claims 13, 14 and 16 (in the Amendment filed March 20, 2006) to recite the step of repeating steps (A) and (B) on a selected DNA molecule "that is different from the selected portion of (B)." The Examiner suggests that the claim language encompasses methods where the testing is (i) conducted on two different regions and (ii) on two different portions of the same region. The Examiner notes support at pages 15-17 for testing on five different regions of a 900 base pair sequence, but contends there is no support for testing on different portions of the same region.

Applicants respectfully traverse the Examiner's position for the following reasons.

Applicants note that the claims recite methods for determining whether a "selected DNA molecule" encodes a gene expression region. Thus, the claims are directed to selecting a particular DNA molecule to be assayed.

As recited in step (B) of claims 13 and 14, and step (b) of claim 16, RNA transcripts are screened for an RNA transcript that corresponds to a "selected portion" of the selected DNA molecule. Thus, the claims are further directed to screening for an RNA transcript that corresponds to a particular portion of the DNA molecule. For example, if the selected DNA

molecule consisted of 1000 nucleotides, the selected portion would be a nucleotide sequence within the 1000 nucleotides, e.g., a portion consisting of nucleotides 200-300.

Finally, as recited in step (C) of claims 13 and 14, and step (c) of claim 16, RNA transcripts are screened for an RNA transcript that corresponds to a "selected portion" of the selected DNA molecule that is different from the selected portion screened in the previous step. For example, if nucleotides 200-300 were the selected portion of step (B), the selected portion of step (C) would be any portion of the selected DNA molecule other than nucleotides 200-300.

The claims are thus directed to screening for RNA transcripts that correspond to different selected portions of the same selected DNA molecule.

While the Examiner states that the claims "encompasses methods in which (i) a region is selected for testing and then the testing is repeated on an entirely different region", Applicants respectfully note that there is no support in the claims for such an interpretation. The claims make clear that the screening method is repeated using two different portions of the same selected DNA molecule. The claims do not support the Examiner's interpretation that the screening method can be repeated on two different selected DNA molecules. As recited in step (C) of claims 13 and 14, and step (c) of claim 16, the method is repeated on a different portion of "the" selected DNA molecule, thus making clear that two different selected DNA molecules are not encompassed within the scope of the claims.

Example 1 of the specification fully supports the amendment to claims 13, 14 and 16. Indeed, at page 3 of the Office Action the Examiner states that "the specification teaches that a region [i.e., a selected DNA molecule] composed of 900 base pairs was divided into five specific regions [i.e., five specific portions of the selected DNA molecule] each having 180 base pairs and that primer and probe sets were made for each region [i.e., each portion of the selected DNA molecule]." Thus, there is support in the specification for a method where the screening is repeated for a different portion of the same selected DNA molecule.

Further support is found in the specification at page 5, line 23, through page 6, line 2, where it is stated that the screening method can be repeatedly carried out on the selected DNA

molecule. Example 1 of the specification discussed above makes it clear that such repetition can be conducted on different portions of the same selected DNA molecule.

In view of these comments, Applicants respectfully assert that no new matter has been added, and respectfully request reconsideration and withdrawal of this rejection.

B. At page 4 of the Office Action, claims 13-16 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite.

(1) The Examiner states that the phrase "that is different from the selected portion of (B)" does not clearly identify whether the claimed methods require one to select a region to be tested and then repeat the method on an entirely different region, or if the method requires one to select a region to be tested and then repeat the method using the same region but a different portion of that region.

Applicants respectfully traverse the Examiner's position for the following reasons.

As explained above, the claims clearly recite the selection of a DNA molecule ("a selected DNA molecule"), the screening of a portion of the selected DNA molecule (step (B) of claims 13 and 14, and step (b) of claim 16), and then repeating the screening on a different portion of "the" selected DNA molecule (step (C) of claims 13 and 14, and step (c) of claim 16). Thus, it is clear that there is one selected DNA molecule and that two different portions of the selected DNA molecule are screened.

As the claims are definite as written, Applicants respectfully request reconsideration and withdrawal of this rejection.

(2) The Examiner also states that the term "corresponding" in the phrase "corresponding to a selected portion of" is not an art recognized term to describe the relationship between two nucleic acid sequences or two amino acid sequences. Specifically, the Examiner contends that it would not be clear as to whether a corresponding nucleic acid refers to a nucleic acid residue at the same position or to one which is at a nearby position, or whether it refers to a similar nucleic acid residue or the same nucleic acid residue at any position.

Applicants respectfully traverse the Examiner's position for the following reasons.

Because an RNA molecule has the same sequence as the DNA molecule which encodes it (with the exception of uracil in place of tyrosine), the term "corresponding" is an art recognized term to describe the relationship between an RNA molecule and the DNA molecule that encodes it.

However, in an effort to address the Examiner's concern and make the claims more clear, included herewith is an amendment to claims 13 and 14 such that these claims now recite "an RNA transcript comprising a nucleotide sequence corresponding to a selected portion of said selected DNA molecule."

In view of the comments above and the amendments to the claims, the claims are definite as written and Applicants respectfully request reconsideration and withdrawal of this rejection.

(3) The Examiner further states that the phrase "a selected portion of" is not clearly defined in the specification and that there is no art recognized definition of this phrase. Specifically, the Examiner reasons that it would be unclear as to whether the phrase refers to any portion of any DNA sequence that has been selected by virtue of amplifying it or a portion of a specific DNA sequence.

Applicants respectfully traverse the Examiner's position and assert that the claims are clear and definite as written. Applicants note that upon choosing a selected DNA molecule, one practicing the recited methods would then select of portion of the selected DNA molecule for which to screen the RNA transcripts. For example, if the selected DNA molecule is 1000 nucleotides in length, and one wished to determine whether the portion of the DNA molecule consisting of nucleotides 200-300 encodes a gene expression region, the portion consisting of nucleotides 200-300 would be the "selected portion of" the selected DNA molecule.

As the claims are definite as written, Applicants respectfully request reconsideration and withdrawal of this rejection.

C. At page 5 of the Office Action, the Examiner states that that claims 13, 14 and 16 are indefinite because the goal of the claimed method and the final step do not agree, and thus it is unclear as to whether the claims recite methods for determining whether a selected DNA

molecule encodes a gene expression region or whether the claims recite methods for detecting an amplification product.

Included herewith is an amendment to the claims such that the goal of the claimed method and the final step are in agreement.

In view of the amendment to the claims, the claims are definite as written and Applicants respectfully request reconsideration and withdrawal of this rejection.

II. Rejection of Claims Under 35 U.S.C. §102

At page 5 of the Office Action, claim 16 is rejected under 35 U.S.C. §102(b)[1] as being anticipated by Lockhart et al. (U.S. Patent No. 6,040,138).

Included herewith is an amendment to the claims such that claim 16 has been canceled, thus making this rejection moot.

In view of the cancellation of claim 16, reconsideration and withdrawal of this rejection are respectfully requested.

III. Rejection of Claims Under 35 U.S.C. §103

A. At page 7 of the Office Action, claim 13 is rejected under 35 U.S.C. §103(a) as being unpatentable over Davey et al. (U.S. patent No. 5,409,818) in view of Cao (U.S. Patent No. 6,582,906).

At pages 8-10 of the Office Action, the Examiner indicates the location of support in Davey et al. for each element of Applicants' claim 13. The Examiner admits that Davey et al. does not teach repeating the method on a different portion of the selected DNA molecule.

The Examiner states that Cao teaches a method for analyzing gene expression in which the method steps are repeated using a different portion of a selected DNA molecule. The Examiner explains that because Cao teaches that the method is repeated once or multiple times,

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[1] The Examiner appears to mistakenly cite to "103(b)" at page 6 of the Office Action, rather than 102(b).

each round of the method for amplifying a population of nucleic acids involves producing multiple copies of sense RNA from double-stranded DNA, and each time the method is repeated the starting population of RNA is different and therefore a population of different double-stranded DNA sequences is produced.

Applicants respectfully traverse the Examiner's position because the Examiner has not established a *prima facie* showing of obviousness.

First, Applicants note that the combination of documents cited by the Examiner does not teach each and every element of the rejected claims. The Examiner has admitted that Davey et al. does not teach the repetition step recited in step (C) of claim 13. Cao also does not teach the repetition step. The Examiner's reference to the multiple repetitions of the steps resulting in a different starting population of sense RNA of Cao is not a repetition of the method on a different portion of the DNA molecule. Indeed, in each of the embodiments of Cao, the method requires choosing a specific (selected) nucleic acid sequence and then making single- or double-stranded DNA from the selected nucleic acid sequence. Further steps in the method pertain to fragmentation of the single- or double-stranded DNA. Each embodiment of Cao thus analyzes only one portion of the selected nucleic acid sequence, albeit a portion that encompasses the entire nucleic acid sequence. As such, neither Davey et al. nor Cao, alone or in combination, teaches each and every step of the method recited in claim 13.

Moreover, Cao describes a method for amplifying nucleic acids in a proportional manner in order to analyze the relative amount of plural types of mRNA and cDNA. In contrast, the present invention provides in one embodiment a method for identifying an expression region by repeatedly amplifying and detecting plural "selected portions" in the "selected DNA" and does not provide a method for proportional amplification. Thus, the method of Cao as well as the use and effect of the method are quite different from the present application.

Second, there would have been no motivation to combine the teachings of Davey et al. and Cao. In particular, Davey et al. teach a method of amplifying a specific nucleic acid sequence. Thus, one practicing the invention of Davey et al. starts with a small amount of a selected nucleic acid sequence, and obtains a larger quantity of the selected nucleic acid

sequence by practicing the method of Davey et al. Even if Cao taught a method that repeated amplification on a different portion of a specific nucleic acid sequence, the skilled artisan would have had no reason to incorporate such repetition in the method of Davey et al. Once the amplification process has been completed, the method of Davey et al. is complete. While it is conceivable that the skilled artisan could selected a second group of primers and repeat the amplification process on the selected nucleic acid sequence, there would be no reason for doing so. Thus there would have been no motivation to combine the teachings of Davey et al. and Cao on this basis.

As the Examiner has not established a *prima facie* showing of obviousness, Applicants respectfully request reconsideration and withdrawal of this rejection.

B. At page 13 of the Office Action, claims 14 and 15 are rejected under 35 U.S.C. §103(a) as being unpatentable over Davey et al. in view of Cao and in further view of Wittwer et al. (U.S. Patent No. 6,503,720 B2).

The Examiner relies on Davey et al. and Cao for the reasons stated above. The Examiner admits that neither reference teaches the detection of the amplified product using an oligonucleotide probe labeled with an intercalating fluorescence dye or one having a differential fluorescence characteristic.

The Examiner states that Wittwer et al. teaches such an intercalating probe in the teaching of PCR amplification and subsequent SYBR green detection, and further teaches an intercalating fluorescence dye having a fluorescence character in the teaching of the Taq Man principle to detect amplification. The Examiner concludes that it would have been *prima facie* obvious to a skilled artisan to combine the method of Davey et al and Cao, with Wittwer et al.

As explained above, the Examiner has not established a *prima facie* showing of obviousness with regard to Davey et al. and Cao. Witter et al. does not provide the missing step of Davey et al. and Cao, nor does it provide motivation to combine the cited publications.

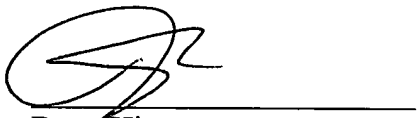
Accordingly, the Examiner has also not established a *prima facie* showing of obviousness of claims 14 and 15 over Davey et al. in view of Cao and in further view of Wittwer et al. Applicants therefore respectfully request reconsideration and withdrawal of this rejection.

IV. Conclusion

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,



SUGHRUE MION, PLLC
Telephone: (202) 293-7060
Facsimile: (202) 293-7860

WASHINGTON OFFICE
23373
CUSTOMER NUMBER

Drew Hissong
Registration No. 44,765

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